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Mitral Balloon Valvotomy for Patients With Mitral Stenosis in Atrial Fibrillation

Immediate and Long-Term Results

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OBJECTIVES The purpose of this study was to examine the effect of atrial fibrillation (AF) on the immediate and long-term outcome of patients undergoing percutaneous mitral balloon valvuloplasty (PMV).

BACKGROUND There is controversy as to whether the presence of AF has a direct negative effect on the outcome after PMV.

METHODS The immediate procedural and the long-term clinical outcome after PMV of 355 patients with AF were prospectively collected and compared with those of 379 patients in normal sinus rhythm (NSR).

RESULTS Patients with AF were older (62 ± 12 vs. 48 ± 14 years; $p < 0.0001$) and presented more frequently with New York Heart Association (NYHA) class IV (18.3% vs. 7.9%; $p < 0.0001$), echocardiographic score >8 (40.1% vs. 25.1%; $p < 0.0001$), calcified valves under fluoroscopy (32.4% vs. 18.8%, $p < 0.0001$) and with history of previous surgical commissurotomy (21.7% vs. 16.4%; $p = 0.0002$). In patients with AF, PMV resulted in inferior immediate and long-term outcomes, as reflected in a smaller post-PMV mitral valve area (1.7 ± 0.7 vs. 2 ± 0.7 cm^2; $p < 0.0001$) and a lower event free survival (freedom of death, redo-PMV and mitral valve surgery) at a mean follow-up time of 60 months (32% vs. 61%; $p < 0.0001$). In the group of patients in AF, severe post-PMV mitral regurgitation (≥3+) ($p = 0.0001$), echocardiographic score >8 ($p = 0.004$) and pre-PMV NYHA class IV ($p = 0.046$) were identified as independent predictors of combined events at follow-up.

CONCLUSIONS Patients with AF have a worse immediate and long-term outcomes after PMV. However, the presence of AF by itself does not unfavorably influence the outcome, but is a marker for clinical and morphologic features associated with inferior results after PMV. (J Am Coll Cardiol 1999;34:1145–52) © 1999 by the American College of Cardiology

Percutaneous mitral balloon valvuloplasty (PMV) has been established as an alternative to surgical mitral commissurotomy in the treatment of patients with symptomatic mitral stenosis (1–12). Several studies have demonstrated that this technique provides sustained clinical and hemodynamic improvement in a selected group of patients with mitral stenosis. Certain clinical and morphologic factors such as age (7,10,11,13), history of previous surgical commissurotomy (7,10,11,14,15), presence of calcification under fluoroscopy (10,11,13,16), echocardiographic score (10,11,15, 17–22), New York Heart Association (NYHA) class IV at presentation (10,11,13,15,17,21) and the presence of severe tricuspid regurgitation (23), have been identified as predictors of immediate and long-term outcome after PMV. The development of atrial fibrillation (AF) is a common and important sequelae in patients with mitral stenosis, and it is associated with hemodynamic and clinical decompensation. Previous surgical studies have demonstrated that the presence of AF is associated with suboptimal immediate and long-term outcome after surgical mitral commissurotomy (24–30). However, there is controversy as to whether AF is an important independent predictor of the immediate and long-term outcome of patients undergoing PMV. Thus, the purpose of this study was to address this important clinical issue by evaluating the effect of AF on the immediate and long-term outcome of PMV in a large cohort of consecutive patients undergoing the procedure at the Massachusetts General Hospital.

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Abbreviations and Acronyms

AF	=	atrial fibrillation
EBDA/BSA	=	effective balloon dilating area/body surface area
MVR	=	mitral valve replacement
NSR	=	normal sinus rhythm
NYHA	=	New York Heart Association
PMV	=	percutaneous mitral balloon valvuloplasty
QP/QS	=	pulmonary to systemic flow ratio

METHODS

Study population. The study group included 734 consecutive patients who underwent PMV at the Massachusetts General Hospital between July 1986 and March 1997. Of these 734 patients, 355 (48.4%) had AF at the time of the procedure and 379 (51.6%) had normal sinus rhythm (NSR). All patients were screened clinically and by transthoracic echocardiography. Patients with AF and those with previous embolic events had undergone anticoagulation with warfarin for at least three months before consideration for PMV. Transesophageal echocardiography was performed in patients with a suboptimal transthoracic study, in those with a history of a previous embolic event and in those with a possible left atrial thrombus by the transthoracic study. Patients with left atrial thrombus were treated with warfarin for at least two to three months, and PMV was performed only if resolution of the left atrial thrombus was demonstrated by repeat transesophageal echocardiography.

PMV procedure. All patients underwent PMV using the transseptal antegrade technique as previously described (1–3), after informed consent was obtained. The double-balloon technique was used with 621 patients and the Inoue technique with 113 patients. The balloon combination in the double-balloon technique was selected on the basis of effective balloon dilating area/body surface area ratio (EBDA/BSA), so that this ratio was >3.3 but less than 4 cm^2/m^2 (31,32). The maximum volume of the Inoue balloon used was determined by the equation: maximum balloon volume (mm) = (patient's height (cm)/10) + 10 (32). Before and after PMV, right and left heart pressure measurements, including simultaneous left atrial and left ventricular pressures and cardiac output, were performed. Oxygen saturation of blood samples from the superior vena cava, pulmonary artery and the aorta were measured before and after PMV. Cardiac output was determined by the thermodilution technique. However, where there was evidence of left to right shunting (step up in oxygen saturation between the right atrium and pulmonary artery ≥7%), or when significant tricuspid regurgitation was present by physical examination or echocardiography, cardiac output was calculated according to the Fick principle. In the presence of left to right shunting, the oxygen content of the blood sample from the superior vena cava was used as the mixed venous blood sample, and oxygen consumption was measured by an MRM-2 oxygen consumption monitor (Waters Instrument Inc., Rochester, Minnesota). The mitral valve area was calculated using the Gorlin formula. Left ventriculography was performed in all patients before and after PMV to assess the severity of mitral regurgitation using the Sellers classification (33).

Data collection and definitions. All data were prospectively collected and entered into a computerized database (InterCard, Massachusetts General Hospital, Boston, Massachusetts) (34). Demographic and clinical variables included age, gender, body surface area, New York Heart Association (NYHA) functional class at presentation, presence of AF and previous surgical commissurotomy. Laboratory variables included the echocardiographic score, pre- and post-PMV severity of mitral regurgitation according to the Sellers classification using contrast left ventriculography and the presence of fluoroscopically visible mitral valve calcification, which was graded from 0 to 4, as previously described (16). Procedural-related variables included the type of technique (double balloon vs. Inoue), EBDA/BSA and the following hemodynamic variables before and after PMV: mean pulmonary artery and left atrial pressures, mean mitral valve gradient, cardiac output and calculated mitral valve area.

Prospectively collected procedure related complications included death, mitral valve replacement (MVR), pericardial tamponade, thromboembolism, third-degree atrioventricular block, post-PMV mitral regurgitation ≥3+ and left to right shunt with a pulmonary/systemic ratio (QP/QS) >1.5:1. Procedure-related death was defined as in-hospital death that was directly related to the PMV procedure. Successful outcome of PMV was defined as a post-PMV mitral valve area ≥1.5 cm^2, without >2+ increase in the severity of mitral regurgitation, and post-PMV mitral regurgitation <3+ and without left to right shunt with QP/QS >1.5:1 after the procedure (18).

Follow up. Follow-up information was obtained by trained medical personnel using direct telephone interviews with the patients or follow-up visits by physicians. This information included survivorship, MVR, redo PMV and clinical evaluation according to the NYHA classification of congestive heart failure symptoms. The interviewer was blinded to the procedural variables and immediate outcome after PMV. When necessary, local physicians were contacted for further information and medical records were reviewed.

Statistical analysis. Continuous variables are expressed as mean ± standard deviation (SD), and categorical variables as percent. Student *t* test and chi-square analysis were carried out for comparison of continuous and categorical variables, respectively. p Values ≤0.05 were considered significant. Demographic, clinical, echocardiographic, procedural and angiographic variables were tested to determine significant ($p < 0.05$) univariate correlates of immediate success in both the overall and in the AF groups. Multiple stepwise logistic regression analyses of these significant variables were performed to identify independent predictors of immediate success in the overall group of patients and in the group of patients in AF.

Kaplan-Meier estimates were used to determine total survival and event-free survival (survival with freedom from MVR and redo PMV) for both groups of patients and compared by log rank test. Cox proportional hazards regression analyses using backward elimination were used to identify independent correlates of mortality and event-free survival in the AF group. Kaplan-Meier plots with log rank test of demographic, clinical and procedural variables were generated to determine potential confounders of the relationship between AF and mortality and between AF and event-free survival. All variables with significant differences in mortality or event-free survival by log rank test were entered into separate proportional hazards models. The variables included in the analyses were age, gender, NYHA functional class at presentation, history of previous surgical commissurotomy, fluoroscopic presence of calcium ≥2+, echocardiographic score, technique of PMV, pre- and post-PMV mitral valve area, pre-PMV mitral regurgitation ≥1+, post-PMV mitral regurgitation ≥3+ and pre- and post-PMV mean pulmonary artery pressure. All variables were initially included in the regression equations. The least significant variable was eliminated first from the models, and the remaining variables were examined again to determine the next least significant variable for removal. This procedure was continued with removal of variables in a stepwise fashion until only significant variables ($p \leq 0.05$) remained in the models. The models were also tested by forward stepping elimination yielding the same independent predictors. All analyses were performed using SAS software version 6.10 (SAS Institute, Cary, North Carolina).

RESULTS

Preprocedural clinical and morphologic variables. Baseline demographic and clinical characteristics of the two groups of patients are shown in Table 1. Patients in AF were older (62 ± 12 vs. 48 ± 14 years, $p < 0.0001$) and presented more frequently with NYHA functional class IV (18.3% vs. 7.9%, $p < 0.0001$), history of previous surgical commissurotomy (21.7% vs. 16.4%, $p = 0.0002$), ≥2+ grade of mitral calcification by fluoroscopy (32.4% vs. 18.8%, $p < 0.0001$), echocardiographic score >8 (40.1% vs. 25.1%, $p < 0.0001$) and pre-PMV mitral regurgitation ≥1+ (51.4% vs. 38.8%, $p = 0.0006$).

Hemodynamic variables. Hemodynamic findings before and after PMV are shown in Table 2. Before PMV, patients in AF had lower pre-PMV mitral valve area (0.86 ± 0.3 vs. 0.94 ± 0.3 cm^2, $p = 0.0002$). After PMV, patients in AF had significantly lower post-PMV mitral valve area (1.7 ± 0.7 cm^2 vs. 2.0 ± 0.7 cm^2, $p < 0.0001$). In addition, the mean pulmonary artery (31 ± 10 vs. 27 ± 11 mm Hg, $p < 0.0001$) and mean left atrial (17 ± 6 vs. 15 ± 6 mm Hg, $p < 0.0001$) pressures were significantly higher after PMV in the AF group. There was no significant difference in the type of technique of PMV (double balloon: 86.5% in the AF group and 82.9% in the NSR group, p = NS) or the EBDA/BSA (AF group: 3.65 ± 0.5, NSR group: 3.67 ± 0.5, p = NS) between the two groups.

Table 1. Baseline Characteristics

	AF (n = 355)	NSR (n = 379)	p Value
Age	62 ± 12	48 ± 14	< 0.0001
Female gender	282 (80%)	319 (84%)	NS
NYHA			
Class I	1 (0.3%)	5 (1.3%)	NS
Class II	65 (18.3%)	119 (31.4%)	< 0.0001
Class III	224 (63.1%)	225 (59.3%)	NS
Class IV	65 (18.3%)	30 (7.9%)	< 0.0001
Echo score ≤8	212 (59.9%)	284 (74.9%)	< 0.0001
Echo score >8	142 (40.1%)	95 (25.1%)	< 0.0001
Fluoroscopic calcium ≥2+	114 (32.4%)	71 (18.8%)	< 0.0001
Prior commissurotomy	77 (21.7%)	43 (16.4%)	0.0002
Mitral regurgitation 1+	145 (41.2%)	133 (35.4%)	0.003
Mitral regurgitation 2+	34 (9.6%)	12 (3.2%)	0.0003

All data are expressed as mean value ± SD or number (%) of patients.
AF = atrial fibrillation; NS = not significant; NSR = normal sinus rhythm; NYHA = New York Heart Association.

Table 2. Hemodynamic Characteristics

	AF (n = 355)	NSR (n = 379)	p Value
MG pre-PMV (mm Hg)	13 ± 5	16 ± 6	< 0.0001
MG post-PMV (mm Hg)	5 ± 3	5 ± 3	NS
CO pre-PMV (liter/min)	3.4 ± 0.9	4.3 ± 1.1	< 0.0001
CO post-PMV (liter/min)	4 ± 1	4.9 ± 1.3	< 0.0001
MVA pre-PMV (cm^2)	0.86 ± 0.3	0.94 ± 0.3	0.0002
MVA post-PMV (cm^2)	1.7 ± 0.7	2.0 ± 0.7	< 0.0001
PA pre-PMV (mm Hg)	37 ± 12	36 ± 14	NS
PA post-PMV (mm Hg)	31 ± 10	27 ± 11	< 0.0001
LA pre-PMV (mm Hg)	24 ± 7	25 ± 7	NS
LA post-PMV (mm Hg)	17 ± 6	15 ± 6	< 0.0001
EBDA/BSA (cm^2/m^2)	3.65 ± 0.5	3.67 ± 0.5	NS
Technique			
Double balloon	307 (86.5%)	314 (82.9%)	NS
Inoue	48 (13.5%)	65 (17.1%)	NS

AF = atrial fibrillation; CO = cardiac output; EBDA/BSA = effective balloon dilating area/body surface area; LA = mean left atrium pressure; MG = mitral gradient; MVA = mitral valve area; NSR = normal sinus rhythm; PA = mean pulmonary artery pressure; PMV = percutaneous mitral balloon valvotomy.

Immediate outcome and complications. The immediate procedural results and in-hospital outcomes are shown in Table 3.

Procedural success. Patients in the AF group have a lower procedural success (61.1% vs. 76.1%, $p < 0.0001$). Univariate predictors of procedural success in the AF group

Table 3. In-Hospital Events

	AF (n = 355)	NSR (n = 379)	p
Procedural success	212 (61.1%)	284 (76.1%)	< 0.0001
Procedural death	4 (1.1%)	0 (0%)	NS
In-hospital death	11 (3.1%)	2 (0.5%)	0.01
MR grade post-PMV			
3+	25 (7.2%)	20 (5.4%)	NS
4+	9 (2.6%)	15 (4%)	NS
Emergent MVR	4 (1.1%)	5 (1.3%)	NS
In-hospital MVR	10 (2.8%)	14 (3.7%)	NS
Pericardial tamponade	4 (1.1%)	2 (0.5%)	NS
AV block	0	2 (0.5%)	NS
QP/QS >1.5	22 (6.2%)	19 (5%)	NS
Thromboembolism	7 (2%)	3 (0.8%)	NS

AF = atrial fibrillation; AV = atrio-ventricular; MR = mitral regurgitation; MVR = mitral valve replacement; NSR = normal sinus rhythm; PMV = percutaneous mitral balloon valvotomy; QP/QS = pulmonary to systemic flow ratio.

included age, male gender, history of previous commissurotomy, NYHA functional status at presentation, fluoroscopic mitral valve calcification, echocardiographic score, pre-PMV mitral valve area, pre-PMV mitral regurgitation and pre-PMV mean pulmonary artery pressure. Multiple stepwise logistic regression analysis identified pre-PMV mitral valve area ($p \leq 0.0001$), echocardiographic score ≤8 ($p = 0.001$), male gender ($p = 0.038$) and absence of previous surgical commissurotomy ($p = 0.048$) as independent predictors of procedural success in patients in AF.

In the overall population, the absence of AF was identified as univariate predictor of procedural success ($p = 0.0001$). Other univariate predictors included younger age ($p = 0.0001$), male gender ($p = 0.0003$), absence of previous commissurotomy ($p = 0.0078$), lower NYHA functional status at presentation ($p = 0.0001$), lower fluoroscopic mitral valve calcification ($p = 0.0001$), lower echocardiographic score ($p = 0.0001$), the technique of (double-balloon technique; $p = 0.05$), larger pre-PMV mitral valve area ($p = 0.0001$), lower pre-PMV mitral regurgitation ($p = 0.0001$) and lower pre-PMV mean pulmonary artery pressure ($p = 0.001$). However, the presence of AF was not an independent predictor of success. Multiple stepwise logistic regression analysis identified pre-PMV mitral valve area (odds ratio [OR] 138, confidence intervals [CI] 43.8 to 466, $p < 0.0001$), echocardiographic score ≤8 (OR 1.92; CI 1.26 to 2.94, $p = 0.002$), male gender (OR 2.32; CI 1.37 to 4.16, $p = 0.002$), absence of previous surgical commissurotomy (OR 1.79; CI 1.09 to 2.94, $p = 0.01$) and younger age (OR 6.25; CI 2.5 to 16.6, $p = 0.0002$) as independent predictors of procedural success.

In-hospital mortality. There were 13 (1.8%) in-hospital deaths, and 4 (0.5%) of them were procedure-related deaths. The four procedure related deaths occurred as follows: one patient who was brought to the catheterization laboratory in cardiogenic shock who underwent emergent PMV and died despite a technically successful and uncomplicated procedure; Another patient who died due to left ventricular perforation and development of tamponade 12 h after PMV; a third patient who died during emergent MVR from intractable right ventricular failure (11) and a fourth patient who presented with cardiogenic shock due to severe aortic and mitral stenosis, underwent emergent PMV and percutaneous aortic valvuloplasty and died due to persistent cardiogenic shock and severe mitral regurgitation. The causes of the other nine in-hospital deaths were the following. One patient died suddenly one day after PMV with the autopsy showing an acute inferior wall myocardial infarction; one patient died from electromechanical dissociation after percutaneous aortic valvotomy, which had been undertaken 24 h after PMV; another patient who was not a surgical candidate died from persistent cardiogenic shock within 24 h after a suboptimal compassionate PMV; one patient died from complications after surgical treatment of a subdural hematoma; one patient with end stage chronic obstructive pulmonary disease died from respiratory failure; and four patients died from multisystem organ failure due to sepsis unrelated to PMV. Although all of the procedure-related deaths occurred in the AF group, this difference was not statistically significant. However, the total in-hospital mortality was higher in the AF group (3.1% vs. 0.5%, $p = 0.01$).

Mitral regurgitation. There were no differences between the AF and NSR groups in the incidence of 3+ (7.2% vs. 5.4%, p = NS) or 4+ (2.6% vs. 4%, p = NS) post-PMV mitral regurgitation as assessed by left ventriculography using the Sellers criteria.

MVR. Twenty-four patients (3.2%) underwent MVR during their hospitalization. Eighteen patients underwent MVR due to development of severe mitral regurgitation (3+ or 4+) after PMV. Two patients underwent MVR during surgical treatment for pericardial tamponade and ongoing hemodynamic deterioration despite pericardiocentesis. In one patient, the pulmonary artery was entered during transseptal catheterization, requiring surgical removal of the catheter and MVR. Finally, three patients underwent MVR due to suboptimal post-PMV mitral valve area. Emergent MVR (less than 24 h after PMV) was required in nine (1.2%) patients. There were no significant differences in the incidence of emergent (1.1% vs. 1.3%, p = NS) or total in hospital MVR (2.8% vs. 3.7%, p = NS) between the AF and NSR groups.

Other complications. Pericardial tamponade occurred in 6 patients (4 patients [1.1%] in the AF group and 2 patients [0.5%] in the NSR group, p = NS). As described earlier, one patient developed tamponade from left ventricular perforation. Two patients continued to have hemodynamic deterioration despite emergent pericardiocentesis and required emergent surgical drainage. The other three patients were successfully treated with pericardiocentesis in the catheterization laboratory and the PMV was completed successfully. A left to right shunt with a pulmonary to systemic flow ratio >1.5:1 was detected in 22 (6.2%) patients in AF versus 19 (5%) of the patients in NSR group (p = NS).

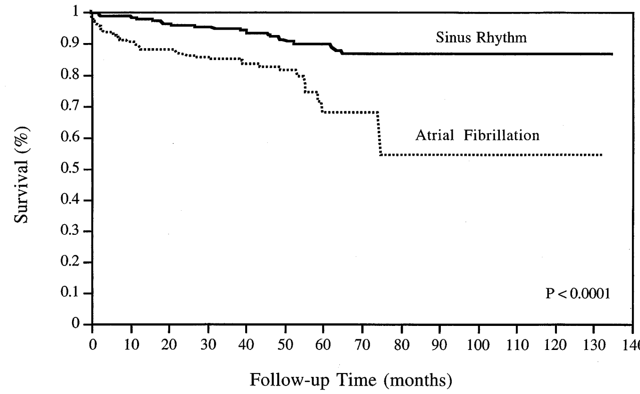
Thromboembolic events occurred in 10 (1.3%) of the overall population: seven (2%) occurred in the AF group and three (0.8%) in the NSR group (p = NS). A cerebrovascular event occurred in five patients, with four of them having complete neurologic recovery at the time of discharge. Four patients had embolism to the lower extremities, requiring surgical intervention. Finally, one patient had an embolic non-Q wave myocardial infarction. He was treated conservatively and had normal left ventricular function at discharge. Finally, two (0.3%) of the patients in the NSR group developed complete atrioventricular block; one responded to atropine administration, and the other required temporary pacemaker insertion for 24 h.

Clinical follow up. Clinical follow up information was available in 672 (91.6%) of the overall patient population at a median follow up time of 66.2 ± 0.9 months. The follow up was completed in 329 (92.7%) of the patients in the AF group and 343 (90.5%) of the patients in the NSR group. In the AF group, cumulative events included 51 deaths, 79 MVR and 20 redo PMV, accounting for a total of 150 patients with combined events (death, MVR or redo PMV. Of the remaining 179 patients that were free of combined events, 163 (91.1%) were in NYHA class I or II and 16 (8.9%) patients were in class III or IV. In the NSR group, cumulative events included 26 deaths, 81 MVR and 21 redo PMV, accounting for a total of 128 patients with combined events at follow-up. Of the remaining 215 patients that were free of any event, 199 (92.6%) were in NYHA class I or II and 16 (7.4%) were in class III or IV.

Figure 1 shows estimated actuarial total survival curves for patients in AF and NSR. Actuarial survival rates throughout the follow-up period were significantly better in patients in NSR than those in AF. Survival rates were 89.4% for the NSR group and 68% for the AF group at a mean follow-up time of 60 months (p < 0.0001). Freedom from MVR (72.3% vs. 56.9%; p = 0.02) and freedom from redo PMV (94.3% vs. 83.3%; p = 0.03) at 60-month follow-up were also significantly higher for patients in the NSR group.

Estimated actuarial event-free survival curves (no death, MVR or redo PMV) are shown in Figure 2. Event-free survival rates were significantly higher in the NSR group throughout the follow-up period. At a mean follow-up time of 60 months, event-free survival was 61% for the NSR group and 32% for the AF group (p < 0.0001).

Cox regression analysis identified post-PMV mitral regurgitation ≥3+ (p = 0.0001), echocardiographic score >8 (p = 0.004) and pre-PMV NYHA class IV (p = 0.046) as independent predictors of combined events at long-term follow-up in the AF group. Furthermore, Cox regression analysis identified pre-PMV NYHA functional class IV

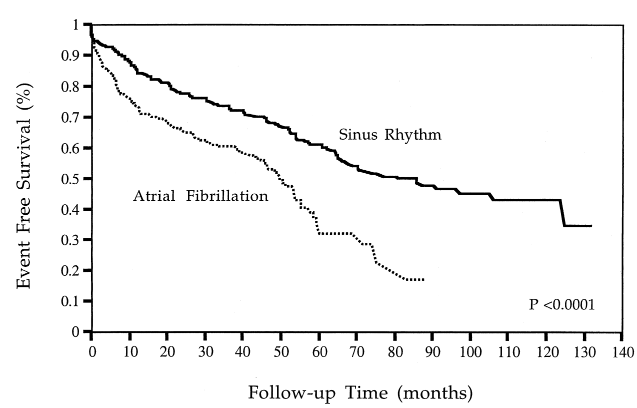


NSR	343	279	236	197	164	131	99	73	60	42	30	23	13	5	2
AF	329	230	179	145	109	55	20	10	5	2				1	

Figure 1. Kaplan-Meier survival curves of patients in normal sinus rhythm versus atrial fibrillation after PMV. Numbers at the bottom represent patients alive and uncensored at the end of each of period of observation for 343 patients in NSR **(top)** and 329 patients in AF **(bottom)** entered at the outset of the study. AF = atrial fibrillation; NSR = normal sinus rhythm; PMV = percutaneous balloon mitral valvuloplasty.

(risk ratio [RR] 3.50; CI 1.92 to 6.49; p < 0.0001), age (RR 1.066; CI 1.03 to 1.099) and post-PMV mean pulmonary artery pressure (RR 1.033; CI 1.01 to 1.06) as independent predictors of mortality at long-term follow-up in the AF group.

In the overall patient population, the presence of AF was not an independent predictor of combined events at long-term follow-up. Cox regression analysis identified post-PMV mitral regurgitation ≥3+ (RR 2.88; CI 2.05 to 3.97; p < 0.0001), echocardiographic score ≥8 (RR 1.48; CI 1.12



NSR	343	279	236	197	164	131	99	73	60	42	30	23	13	5	2
AF	329	230	179	145	109	55	20	10	5	2				1	

Figure 2. Kaplan-Meier event-free survival curves of patients in NSR versus AF after PMV. Numbers at the bottom represent patients alive and free of combined events (mitral valve surgery and redo-PMV) uncensored at the end of each of period of observation for 343 patients in NSR **(top)** and 329 patients in AF **(bottom)** entered at the outset of the study. Abbreviations as in Figure 1.

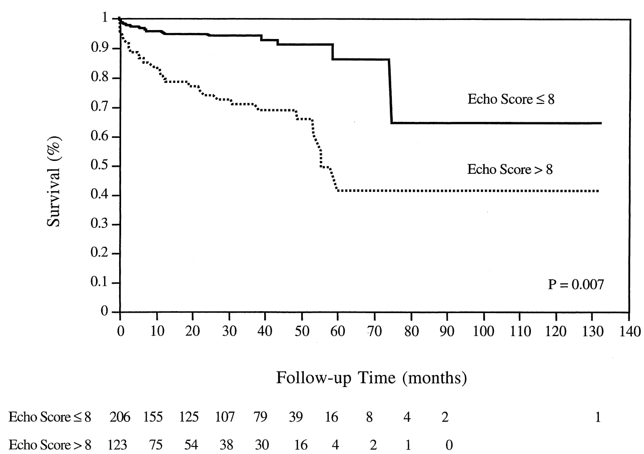


Figure 3. Kaplan-Meier survival curves of patients in AF with echocardiographic score ≤8 and >8 after PMV. Numbers at the bottom represent patients alive and uncensored at the end of each of period of observation for 206 patients in NSR **(top)** and 123 patients in AF **(bottom)** entered at the outset of the study. Abbreviations as in Figure 1.

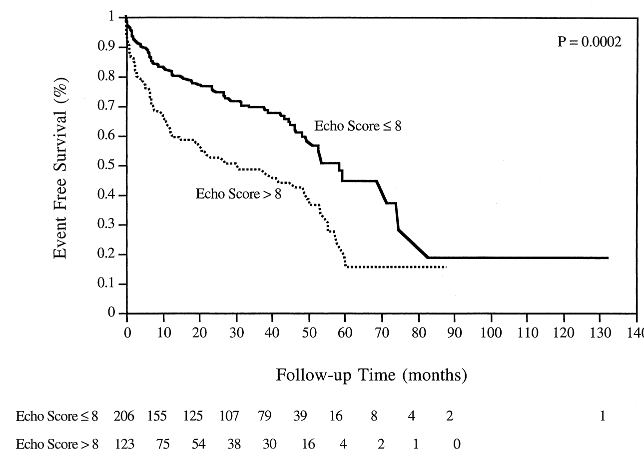


Figure 4. Kaplan-Meier survival and event-free survival curves of patients in AF with echocardiographic score >8 after PMV. Numbers at the bottom represent patients alive and free of combined events (mitral valve surgery or redo-PMV) uncensored at the end of each of period of observation for 206 patients in NSR **(top)** and 123 patients in AF **(bottom)** entered at the outset of the study. Abbreviations as in Figure 1.

to 1.97; $p = 0.005$), age (RR 1.02; CI 1.01 to 1.03; $p < 0.0001$), post-PMV MVA (RR 0.78; CI 0.63 to 0.93; $p = 0.01$) and post-PMV mean pulmonary artery pressure (RR 1.02; CI 1.01 to 1.03; $p = 0.0001$) as independent predictors of combined events at long-term follow-up.

Echocardiographic score, AF and immediate and long-term outcomes. In the AF group, patients with echocardiographic scores ≤8 had a superior immediate success rate (72% vs. 44.5%; $p < 0.0001$) than patients with echocardiographic scores >8. Furthermore, in this group of AF patients, survival (83.5% vs. 37.9%; $p < 0.0001$) and event-free survival (43.5% vs. 16.3%; $p < 0.0001$) at 60-month follow up were significantly higher in patients with echocardiographic scores ≤8 (Figs. 3 and 4). The negative effect of AF in the long-term outcome of patients undergoing PMV is also present in patients with echocardiographic scores ≤8. At a similar follow-up time of 60 months, patients in AF with echocardiographic scores ≤8 had a worse survival (83.5% vs. 93.7%) and event-free survival (43.5% vs. 67.9%) than those patients in NSR with echocardiographic scores ≤8 ($p = 0.0007$).

DISCUSSION

The present study demonstrates that patients with rheumatic mitral stenosis in AF have a worse immediate and long-term outcome after PMV. However, the presence of AF by itself does not unfavorably influence the outcome, but is a marker for clinical and morphologic features associated with inferior results after PMV.

AF and immediate outcome of PMV. Although the presence of AF is not an independent predictor of procedural success, patients in AF have an inferior immediate hemodynamic outcome of PMV as reflected in a lower procedural success rate (61% vs. 76%, $p < 0.0001$) and a smaller post-PMV mitral valve area (1.7 ± 0.7 cm^2 vs. 2 ± 0.7 cm^2, $p < 0.0001$). However, there were not significant differences in the post-PMV incidence of severe mitral regurgitation, or left to right shunting between the two groups of patients. A higher incidence of clinical and morphologic characteristics associated with suboptimal results after PMV in this patient cohort account for these results. Although the presence of AF was associated with higher in-hospital mortality, other procedural complications such as in-hospital MVR, pericardial tamponade and thromboembolic events were similar in the two groups of patients.

AF and long-term follow-up after PMV. The present study also demonstrates that the presence of AF had a negative effect on the clinical follow-up of patients undergoing PMV. Patients with AF had lower survival and event-free survival than patients with NSR. At a mean follow-up time of 60 months, survival and event-free survival were 89.4% and 61%, respectively, for NSR group and only 68% and 32% for the AF group ($p < 0.0001$). Again, the presence of AF was not an independent predictor of event-free survival. Therefore, the inferior immediate and long-term outcome of PMV in patients with mitral stenosis who have AF is more likely related to the presence of clinical and morphologic characteristics associated with inferior results after PMV. In the present study, patients in AF were older and presented more frequently with echocardiographic scores >8, NYHA functional class IV, calcified mitral valves under fluoroscopy and with a previous history of surgical mitral commissurotomy. Previous studies have demonstrated that older age (7,10,11,13,18,21,22), NYHA class IV at presentation (10,11,13,15,17,21) high echocardiographic score (>8) (10,11,15,17–22), history of prior surgical commissurotomy (7,10,11,14,15,18), and fluoroscopically visible mitral valve calcification (10,11,13, 16,18,35) are associated with suboptimal immediate and long-term results of PMV. In addition, the worse immediate hemodynamic outcome of PMV in the AF group contributes to the worse long-term outcome of this group of patients. Smaller post-PMV mitral valve area (21,22,36) and higher post-PMV pulmonary artery pressures (13,21,36) have been identified as important predictors of combined events during long-term follow up after PMV.

Accordingly, it is reasonable to assume that the presence of AF represents a marker for more severe or long-standing mitral stenosis, and it is inevitably associated with clinical and morphologic features that adversely affect the immediate and long-term outcome after PMV. Previous studies have demonstrated that structural changes in the left atrial myocardium are important for the development of AF, and that the prevalence of AF correlates with the severity of myocardial derangement in the left atrium (37–40). The strong association between age and AF in mitral stenosis suggests that the structural changes in the atrial myocardium that predispose to AF are time-dependent. Therefore, the chronicity of the underlying rheumatic disease process in patients with atrial fibrillation is more likely to be associated with more severe mitral valve deformity and calcification.

Predictors of immediate and follow-up results in patients in AF. Although PMV results in a good immediate outcome in only 61% of patients in AF and a five-year event-free survival of 32%, we identified independent predictors that would define a subgroup of patients in the AF group that would have the best chance of immediate success and sustained long-term benefit from PMV. Among these predictors, the echocardiographic score remains the most important independent preprocedural determinant of immediate and long-term outcome and the major factor that the clinician should take into account before recommending PMV in patients with mitral stenosis and AF. A sustained long-term benefit can be predicted primarily by the presence of a low echocardiographic score and a successful PMV procedure. Although the present study demonstrates that patients in AF with echocardiographic scores ≤8 had a worse survival and event-free survival than those patients in NSR with echocardiographic scores ≤8, the presence of AF does not necessarily predict inferior immediate and long-term outcome after PMV. Patients with AF with echocardiographic scores ≤8 have immediate and long-term outcomes comparable with patients in NSR.

Comparison with previous studies. Previous studies on the influence of AF on the immediate success and long-term outcome after PMV have been controversial. We have previously reported that the presence of AF was an independent predictor of suboptimal result after PMV in a smaller group of patients (19,20). The negative influence of AF was also demonstrated in a group of patients with echocardiographic scores ≥10, where AF was the only predictor of sub-optimal result (41), as well as in a subgroup of patients with previous surgical commissurotomy, where AF was a univariate predictor of immediate and short-term outcome. Hung et al. (42) reported that AF was a univariate predictor of suboptimal immediate result but not an independent predictor by multivariate analysis. Iung et al. (43) identified sinus rhythm as univariate predictor of good functional results five years after a successful procedure, but the multivariate analysis failed to demonstrate rhythm as a independent predictor of long-term success. Pan et al. (35) identified the presence of AF as an independent predictor of late success. Conversely, in the larger series from the NHLBI registry of percutaneous balloon mitral commissurotomy, AF was not an independent predictor of procedural success or long-term outcome at 4 years of follow-up (21,44). Other reports also did not reveal any association between AF and suboptimal immediate or long-term outcome after percutaneous balloon valvotomy (4,5,7,17,22). The inconsistency of the results of these studies is more likely explained by the size of the patient population included in each study as well as different baseline clinical and morphologic characteristics of the patients.

Our results agree with previous surgical studies showing the negative influence of AF on the immediate and long-term outcome of patients with mitral stenosis undergoing closed and open surgical commissurotomy for the treatment of symptomatic mitral stenosis. They demonstrated that the presence of AF had an adverse effect on operative mortality and long-term survival and event-free survival after open and closed commissurotomy (24–30) and was, in some of them, an independent predictor of outcome. In a clinical study of 1,000 consecutive cases of mitral stenosis followed up to nine years, Ellis et al. (28) identified the presence of NSR as an important predictor of improvement after closed surgical commissurotomy. In a study of 267 patients followed during 20 years after transventricular commissurotomy, Rihal et al. (29) identified AF as an independent predictor of long-term survival. In the study by Scalia et al. (30) with a follow-up time up to 22 years after closed or open mitral commissurotomy, AF was identified as an univariate predictor of survival and effective palliation.

Conclusions. The present study demonstrated that the presence of AF is associated with inferior immediate and long-term outcome after PMV. Analysis of preprocedural and procedural characteristics revealed that this association is most likely explained by the presence of multiple factors in the AF group that adversely affect the immediate and long-term outcome of PMV. Therefore, the presence of AF should not be the only determinant in the decision process regarding treatment options in a patient with rheumatic mitral stenosis because its presence does not necessarily predict adverse outcome. An echocardiographic score ≤8 primarily identifies a subgroup of patients in AF in whom percutaneous balloon valvotomy is very likely to be successful and provide good long-term results.

Study limitations. Follow-up information was not available in 8.4% of the patient population. Because it is likely that patients may have not received follow up due to an adverse event, this may have affected the results of our study.

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